

4 43. The cell line having the ATCC Accession No. HB 11049 which secretes the monoclonal antibody according to claim ²41.

5 44. The monoclonal antibody or antigen binding fragment according to claim ¹40, wherein the antibody or antigen binding fragment does not bind to P-selectin.

6 45. The monoclonal antibody or antigen binding fragment according to claim ¹40; wherein the antibody or antigen binding fragment selectively binds to L-selectin in humans, sheep, goats, cattle and pigs.

7 46. The monoclonal antibody or antigen binding fragment thereof according to claim ¹40 or ²41 wherein the antibody or antigen binding fragment is further characterized by its ability to specifically inhibit leukocyte rolling on an endothelial cell layer.

8 47. The monoclonal antibody or antigen binding fragment thereof according to claim ¹40 or ²41 wherein the antibody or antigen binding fragment is further characterized by its ability to specifically inhibit lymphocyte homing to peripheral tissues.

9 48. The monoclonal antibody or antigen binding fragment thereof according to claim ¹40 or ²41 wherein the antibody or antigen binding fragment is further characterized by its ability to specifically inhibit an inflammatory response in humans, sheep, cattle and pigs.

10 49. A monoclonal antibody produced by a process comprising:

- (a) immunizing a mammal with an immunogen composed of cells stably expressing E-selectin, cells stably expressing L-selectin or a combination of cells stably expressing E-selectin and cells stably expressing L-selectin;
- (b) fusing lymphocytes from the immunized mammal with myeloma cells;

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(c) selecting hybrid cells that secrete antibodies wherein said antibodies have the characteristic of specifically binding a common antigenic determinant on L-selectin and E-selectin, said binding requires a short consensus repeat domain and said binding simultaneously or individually inhibits E-selectin and L-selectin mediated functions; and

(d) isolating the antibodies.

11 50. The monoclonal antibody according to claim ¹⁰49 wherein the immunogen is a human E-selectin cDNA transfected cell.

12 51. A pharmaceutical composition comprising the monoclonal antibody or antigen binding fragment according to claim ¹40, ²41 or ¹⁰49 and a pharmaceutically acceptable carrier.

13 52. The pharmaceutical composition according to claim ¹²51 further comprising an anti-inflammatory agent selected from the group consisting of: catecholamines, resorcinols, salingenins, ephedrine, glucocorticoids, cromolyn sodium, and anticholinergics.

14 53. A process for producing monoclonal antibodies which specifically bind to a common antigenic determinant on E-selectin and L-selectin comprising:

(a) immunizing a mammal with an immunogen composed of cells stably expressing E-selectin, cells stably expressing L-selectin or a combination of cells stably expressing E-selectin and cells stably expressing L-selectin;

(b) fusing lymphocytes from the immunized mammal with myeloma cells;

(c) selecting hybrid cells that secrete antibodies wherein said antibodies have the characteristic of specifically binding a common antigenic determinant on L-selectin and E-selectin, said binding requires a short consensus repeat domain and said binding

simultaneously or individually inhibits E-selectin and L-selectin mediated functions;

and

(d) isolating the antibodies.

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15 54. The method according to claim ¹⁴53 wherein immunogen is a human E-selectin cDNA transfected cell.

16 55. A method of inhibiting the adhesion of a first cell bearing an E-selectin molecule to a second cell bearing an L-selectin molecule comprising:

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contacting said cells with the antibodies or antigen binding fragments of claim 40 under conditions wherein the antibodies bind to the cells in an amount sufficient to prevent the first cell from binding to the second cell.

17 56. The method according to claim ¹⁶55, in which the monoclonal antibody is EL-246 secreted by a hybridoma having the ATCC Accession No. HB 11049.

18 57. The method according to claim ¹⁶55 wherein the E-selectin and L-selectin bearing cells are at a site of inflammation in a mammal.

19 58. A method of detecting E-selectin and L-selectin bearing cells in biological sample suspected of containing the selectin bearing cells comprising:

- a. contacting the sample with the antibodies or antigen-binding fragments of claim ¹40 or ²41 to form an immune complex with the E-selectin and L-selectin bearing cells, and;
- b. detecting the presence of the immune complex.

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20 59. A method of treating a mammal to inhibit tissue damage occurring at an inflammatory site in any part of the body of a mammal experiencing a leukocyte-mediated inflammatory condition, said method comprising:

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administering *in vivo* a monoclonal antibody according to claim 40¹ or 41² in an amount sufficient to bind specifically to L-selectin and E-selectin molecules expressed on the surface of leukocytes and endothelial cells, respectively, and sufficient to inhibit tissue damage.

21 60. The method according to claim 59²⁰ in which said inflammatory site is located at the vascular endothelial cell interface or subcellular matrix of a body part.

22 61. The method according to claim 59²⁰ in which said inflammatory site involves endothelial tissue of a body part.

23 62. The method according to claim 59²⁰ in which said inflammatory site is in a joint or body part.

24 63. The method according to claim 59²⁰ in which said inflammatory site is the result of a myocardial infarct.

25 64. The method according to claim 59²⁰ in which the monoclonal antibody is administered intravenously at a selected time period prior to or during said inflammatory condition.

26 65. The method according to claim 59²⁰ in which said monoclonal antibody binds to L-selectin and E-selectin expressing cells and does not bind to P-selectin.

27 66. A method of inhibiting an inflammatory response at a site of ischemia-reperfusion injury in a mammal, said method comprising:

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administration of an effective amount of a monoclonal antibody or antigen binding fragment thereof according to claim ~~40~~¹ or ~~41~~², said amount inhibits the inflammatory response at the site of ischemia-reperfusion injury.

18 67. The method according to claim ~~66~~²⁷, wherein the site is selected from the group consisting of a heart, lung, joint, brain, limb, blood vessel, lymph node, spleen, crush injury site, spinal cord or transplantation site.

14 68. The method according to claim ~~66~~²⁷ wherein the ischemic injury is caused by a myocardial infarction, shock, stroke, organ transplantation, crush injury, limb replantation, frostbite or lung ischemia/reperfusion injury.

20 69. The method according to claim ~~66~~²⁷ said amount is effective to inhibit loss of lung function.

31 70. The method according to claim ~~66~~²⁷ wherein the monoclonal antibody is EL-246 which is secreted by a cell line having the ATCC Accession No. HB 11049.

34 71. A method to inhibit leukocyte rolling on an endothelial cell layer comprising:
treatment of the leukocytes or the endothelial cell layer with an amount of the monoclonal antibody or antigen binding fragment according to claim ~~40~~¹ or ~~41~~², said amount is effective to inhibit leukocyte rolling.

37 72. The method according to claim ~~71~~³² wherein the endothelial cell layer is an endothelium lining a lymphatic vessel, artery, vein or postcapillary venules.

39 73. A method to inhibit lymphocyte homing to peripheral tissue of a mammal comprising:

administration of an effective amount of the monoclonal antibody or antigen binding fragment according to claim ~~40~~¹ or ~~41~~², said amount inhibits the homing of lymphocytes from the blood to the peripheral tissue.

REMARKS

Applicant has cancelled all pending claims and submitted herein a new set of claims for the convenience of the Examiner and to assist in the speedy prosecution of the application.

New claims 40 through 73 correspond to the previously pending claims and do not add new matter. The substitute new claims correlate with and finds support from the old claims as follows:

<u>Old Claim</u>	<u>Substitute New Claim</u>
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